REMARKS

Upon entry of the present amendment, claims 20 and 143-222 will be pending. Claims 143-220 have been withdrawn by the Examiner, thus claims 20, 221, and 222 are under examination. Claims 53, 60, 107, and 115 have been cancelled without prejudice previously, and claims 21-142 have been cancelled without prejudice by the present amendment. Claim 20 has been amended to read on the elected invention, namely to recite mutations at a specific residue: position 13. New claim 222 has been added, reciting specific basis residue introducing mutations. Support for new claim 222 can be found throughout the specification as filed, *e.g.*, at page 73, lines 18-20 and at page 39, lines 2-3. Applicants respectfully request that the present amendment be entered and submit that no new matter has been added.

Election/Restrictions

The Examiner withdrew claims 143-220 as allegedly being directed to a non-elected invention and requiring "not only a new species election, but a completely new search of the invention" (Office Action at page 2). Applicants traverse. Claims 143-220 depend from claim 20 and recite additional mutations. If amended claim 20 (reciting a basic residue introducing mutation at position 13) is found allowable, claims that depend from it and recite additional features should also be patentable. Applicants respectfully request that claims 143-220 be examined now, or at least when claim 20 is found to be allowable.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 20, 21, 31, 73, 85 and 221 were rejected as allegedly being indefinite (at page 3 of the Office Action; for completeness, Applicants note that while the Examiner rejected claim 222, it is believed that claim 221 was meant, as no claim 222 was pending before the present amendment). According to the Office, "there is no upper limitation on the number of mutations that may occur" (at page 3). Without conceding to the substance of the rejection, but solely to move the claims toward allowance, claim 20 has been amended to recite an isolated hCG protein comprising a basic residue introducing mutation at position 13 of SEQ ID NO:3.

Applicants submit that amended claim 20 allows a skilled practitioner to interpret its metes and bounds and understand how to avoid infringement, as required by MPEP § 2173.02. The protein is claimed in both structural and functional elements, *i.e.*, reciting a basic residue introducing mutation at position 13 and reciting increased hCG bioactivity. One skilled in the art would understand that a protein with these elements and additional mutations is within the metes and bounds of the claim. Amino acid mutation techniques are known in the art, and skilled practitioners would understand how to introduce and screen for additional mutations. Thus, the proteins claimed in amended claim 20 are definite to those skilled in the art. Claims 221 and 222 depend from claim 20 and are therefore also definite. Claims 21, 31, 73, and 85 have been cancelled. Withdrawal of the indefiniteness rejection is respectfully requested.

Rejections under 35 U.S.C. § 112, First Paragraph

At page 4, the Examiner rejected claims 20, 21, 31, 73, 85, and 222 as allegedly not being enabled (as discussed above, it is believed that claim 221 was meant to be rejected instead of claim 222). According to the Examiner, "the specification, while being enabling for hCGβ having mutation N13X (X being any amino acid, generically), does not reasonably provide enablement for hCGβ having an unspecified additional number of mutations" (at page 4; emphasis added). Applicants disagree. Nonetheless, without acquiescing to the rejection, claim 20 was amended as discussed above to recite an isolated hCG protein comprising a basic residue introducing mutation at position N13.

Based on the specification and the teaching of the art, a skilled practitioner would be able *to make* an isolated hCG protein with a basic residue introducing mutation at position 13. Amino acid mutation techniques are known in the art. Further, the practitioner would be able to introduce additional mutations following routine methods and screen the resulting protein for increased bioactivity without undue experimentation. Examples of evaluating mutants for their bioactivity are provided, *e.g.*, at pages 79-81 of the specification as filed. The specification also allows those skilled in the art *to use* the claimed proteins. For example, at page 82, third and fourth full paragraphs, the specification discusses administration of the claimed proteins for treatment of disorders (e.g., hypogonadotropic hypogonadism), in which hCG is absent or decreased. Thus, a skilled practitioner would be able to make and use the claimed proteins based on the teachings of the specification without undue experimentation.

Claims 221 and 222 depend from claim 20 and are therefore also enabled. Claims 21, 31, 73, and 85 have been cancelled. Withdrawal of all enablement rejections is respectfully requested.

Rejections under 35 U.S.C. § 102(b)

Claims 20, 73, 85, and 222 were rejected as allegedly anticipated by Campbell et al., WO91/16922 (as discussed, it is believed that rejection of claim 221 not claim 222 was meant). The Examiner states that Campbell discloses a species having the substitution N13E (acidic residue) (at page 7). Without conceding to the substance of the rejection, but solely to move the claims toward allowance, Applicants amended independent claim 20 to recite an isolated hCG protein comprising a basic residue introducing mutation at position N13. This amendment renders the anticipation rejections moot and withdrawal of all rejections under Campbell is respectfully requested. Claims 73 and 85 have been cancelled, and claims 221 and 222 depend from amended claim 20.

Rejections under 35 U.S.C. § 103(a)

The Examiner rejected claims 20, 21, 31, 73, 85, and 222 as allegedly being obvious over Moyle, U.S. Patent No. 7,001,597 ("Moyle") in view of U.S. Patent No. 6,486,303 ("Moyle II") or U.S. Patent No. 5,851,997 ("Harris") (at page 7; as discussed, it is believed that rejection of claim 221 not claim 222 was meant). According to the Office, Moyle teaches hCG muteins with substitutions at position N13, wherein the substitution can by any other amino acid (at page 7). Further, the Office states that administration of hCG is known to increase progesterone production (at page 8, citing U.S. Patent No. 4,006,227, "Gallegos"). Applicants disagree with the Examiner's conclusions regarding previously presented claims. Nonetheless, to expedite prosecution, claim 20 has been amended as discussed *supra*. Applicants submit that amended claim 20 and its dependent claims 221 and 222 are not rendered obvious by Moyle, whose disclosed proteins are significantly different from the presently claimed compositions. None of the other references cited cure Moyle's deficiencies.

First, it would not have been obvious to a skilled practitioner to substitute the N13 residue of hCG beta with a basic residue based on Moyle, who discusses indiscriminate types of substitutions. Amended claim 20 does not teach all possible types of N13 mutations, but instead

specifies that they should be basic amino acid substitutions. Generally, out of the twenty amino acids, three are considered basic. Moyle does not offer the motivation to modify it to arrive at the claimed proteins with these few possible mutations, disclosing all possible types of substitutions at N13. Thus, Moyle teaches a genus of mutants but does not disclose the claimed species. Neither Moyle II nor Harris nor Gallegos cure Moyle's deficiencies because none teach basic residue mutations at position N13. The Examiner has not shown otherwise.

Second, it would not have been obvious to obtain hCG beta mutants with increased bioactivity in view of Moyle. Wild type hCG is secreted during pregnancy to help maintain pregnancy (see, e.g., present specification at page 82, lines 8-9). Moyle teaches that the 2a analog of hCG beta (with N13X and N30X mutations) will have anti-LH activity and either facilitate ovulation or terminate pregnancy (Table 1 at col. 43 and Table 2 at col. 46). The actions of analog 2a will depend on the time at which it is administered (col. 41, lines 47-52). Thus, Moyle discusses use of hCG beta mutants with actions antagonistic to those of wild type hCG and thus with decreased bioactivity. Instead, the present claims are drawn to proteins with increased hCG bioactivity. The present specification further states that disorders (e.g., hypogonadotropic hypogonadism) where hCG is absent or decreased can be treated by administering the proteins of the present invention. Therefore, upon reading Moyle, a skilled practitioner would not be motivated to arrive at proteins with increased hCG bioactivity. In fact, Moyle suggests that hCG beta mutants with decreased bioactivity offer many advantages, i.e., inhibition of fertility via termination of pregnancy. Neither Moyle II nor Harris nor Gallegos cure the deficiencies of Moyle. While Gallegos states that HCG is known to induce high levels of progesterone in humans (at col. 12, lines 40-41), the references refers to endogenous hCG with normal activity, not to a mutant version with increased bioactivity. Thus, neither Moyle nor Gallegos, individually or in combination, teach that N13 basic mutation results in hCG beta with increased bioactivity.

In summary, Applicants submit that presently claimed proteins as a whole are not obvious over Moyle and in view of Moyle II, Harris, and Gallegos. Moyle does not teach the specific claimed amino acid mutations that would result in the proteins' increased hCG bioactivity and offers no motivation or reasonable expectation of success to arrive at such proteins. Other cited references do not overcome Moyle's deficiencies. The Examiner has not

shown otherwise and therefore has not established a *prima facie* case of obviousness. Withdrawal of the obviousness rejection is respectfully requested.

CONCLUSION

It is respectfully submitted that the above-identified application is now in a condition for allowance and favourable reconsideration and prompt allowance of these claims are respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

The Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 (with the exception of the issue fee) which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 50-1283. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

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Respectfully submitted,
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